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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,394	03/29/2006	Matti Kivikko	06267.0128	6385

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EXAMINER	
STONE, CHRISTOPHER R	

ART UNIT	PAPER NUMBER
1628	

MAIL DATE	DELIVERY MODE
10/22/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,394	KIVIKKO ET AL.	
	Examiner	Art Unit	
	CHRISTOPHER R. STONE	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 August 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed August 16, 2010, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Status of Claims

Claims 3-8 are pending and under examination.

Rejections Maintained

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 3-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Follath et al (The Lancet, Vol. 360, p. 196-202, 2002) in view of Perrone et al (Clinical Chemistry, 38(10), p. 1933-1953, 1992) and Pagel et al (Cardiovascular Drug Reviews, 14(5), p. 286-316, provided by Applicant).

Claims 3-8 are drawn to a method of treating renal failure and reducing the mortality in a mammal suffering from renal failure comprising administering levosimendan or its metabolite (R)-N-[4-(1,4,5,6- tetrahydro-4-methyl-6-oxo-3-pyridazinyl)phenyl]acetamide, or any of their pharmaceutically acceptable salts.

Follath et al teaches a method of treating heart failure in a human comprising administering levosimendan (abstract). Follath et al further teaches that the administration of levosimendan decreases serum creatinine levels, possibly due to increased organ (e.g. kidney) perfusion (p. 200, left column, 3rd full paragraph). Follath et al does not expressly teach that the method treats severe renal failure or reduces mortality in a mammal suffering from severe renal failure or the periodic or daily administration of levosimendan orally.

Perrone et al teaches that serum creatinine is the most widely used and commonly accepted measurement of renal function and that serum creatinine concentration is inversely proportional to the glomerular filtration rate and renal function (abstract, p. 1934, right column first paragraph and Fig. 1B). That is, a decrease in serum creatinine indicates increased renal function.

Pagel et al et al teaches the daily administration of levosimendan, orally, for the treatment of heart failure (p. 311, first full paragraph, p. 313, 2nd full paragraph). Pagel et

al further teaches that levosimendan has similar pharmacokinetics in patients without renal failure and in patients with severe renal failure (creatinine clearance as low as 8ml/min, p. 304, first paragraph, p. 313, last paragraph).

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time of the instantly claimed invention to orally administer levosimendan to a mammal with severe renal failure in order to treat said renal failure and to reduce the mortality in a mammal suffering from severe renal failure, since administration of the drug was known to result in increased renal function (i.e. to treat renal failure or dysfunction), daily oral administration was taught to be an appropriate schedule/route of administration for the drug and severe renal failure would not have been expected to negate the efficacy of the drug since the pharmacokinetics (e.g. bioavailability) of the drug were not compromised by severely impaired kidney function, thus resulting in the practice of the instantly claimed invention with a reasonable expectation of success.

Response to Arguments

Applicant argues that one of ordinary skill in the art would not have been motivated to treat severe renal failure with levosimendan, since such patients were excluded from the trial of Follath et al. This is found unpersuasive because, while patients with severe renal failure, i.e. not patients with renal insufficiency of a lesser degree, were excluded from the trial testing the efficacy and safety of levosimendan in the treatment of heart failure, it is clear from the study that levosimendan has activity which improves kidney function (i.e. to treat renal failure or dysfunction) , providing motivation to one of ordinary skill in the art to administer the compound for the treatment

of renal failure, e.g. severe renal failure. Furthermore it is noted that only instant claims 7 and 8 are drawn to severe renal failure in particular. Applicant argues that agents that produce vasodilation and increase renal blood flow in subjects with healthy renal function have failed to show benefit in subjects suffering from renal failure and that levosimendan has failed to show benefit in animal models of the condition. This is found unpersuasive because levosimendan is expressly taught to decrease serum creatinine levels in a patient population which does not exclude patients with e.g. moderate renal failure and such activity is the most commonly used and accepted indication of increased renal function, providing motivation to one of ordinary skill in the art to practice the instantly claimed invention, regardless of its potential renal vasodilatory activity and lack of effect in a particular animal model of renal failure.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRISTOPHER R. STONE whose telephone number is (571)270-3494. The examiner can normally be reached on Monday-Thursday, 7:30am-4:00pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on (571) 272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CRS

/Brandon J Fetterolf/
Supervisory Patent Examiner, Art Unit 1628